Effects of a low concentration of isoflurane on contrast sensitivity in volunteers†


Summary

The effects of 0.15% quasi steady-state end-tidal isoflurane on the contrast sensitivity of five healthy volunteers were investigated by measuring their performance in computer generated letter discrimination tasks. A series of letters were displayed on a computer screen so that the luminance of the letter differed from that of the background. Two protocols were used: in the static protocol, the letter remained displayed on the screen until the subject responded, whereas in the dynamic protocol, the letter was displayed for 1/72 s only. Isoflurane significantly decreased contrast sensitivity in both protocols in all subjects. (Br. J. Anaesth. 1998; 81: 176–179)

Keywords: anaesthetics volatile, isoflurane; brain, monitoring, contrast sensitivity

Many different measures have been used in an attempt to find a sensitive, specific and repeatable measure of impairment of neuropsychological function in the recovery phase after general anaesthesia. The oculomotor system is a popular choice because this system can be treated as a “black box” producing highly repeatable, stereotypical movements. It has been shown that inhalation of isoflurane depresses peak saccadic velocity (PSV) and increases saccadic error.1 2 It was postulated that a task involving a higher level of cognitive processing might be more sensitive to the effects of low-dose anaesthesia seen in the recovery period after general anaesthesia. To investigate this, contrast sensitivity was measured in the presence and absence of isoflurane administration by measuring performance in letter discrimination tasks.

Methods

Five healthy anaesthetists were studied. The study was approved by the Hospital Ethics Committee and informed consent was obtained from each subject. The study consisted of a 1-h experimental session; in the first half the subjects breathed oxygen, and in the second half isoflurane in oxygen, titrated to an end-tidal concentration of 0.15%. Practice sessions breathing air were conducted before the study commenced to minimize any learning effect.

CONTRAST SENSITIVITY

Contrast sensitivity can be defined as the ability to see an object against a background. If a subject is asked to identify an object at a different luminance from that of a background, the greater the luminance difference, the easier it is for the subject to correctly identify the object. Contrast is a measure of the difference in luminances, and is defined as

$$\frac{I_{\text{object}} - I_{\text{background}}}{I_{\text{background}}}$$

where \(I\) represents luminance. If the test is repeated a number of times, the probability of correctly identifying the object can be plotted against the contrast, to give a “contrast sensitivity function”, which has the form of a sigmoid curve, the standard psychophysical function.

In this study, letters were displayed on a computer screen at varying luminances relative to background. The subject was informed that the letter displayed was one of 10 pre-selected letters and was asked to guess what it was (fig. 1). The advantages of this procedure are that many repeats are possible, enabling the probability of correctly identifying the letter to be estimated.

BREATHING SYSTEM

Each subject sat in a comfortable chair in front of the computer screen. They breathed room air for training runs and for experimental runs either oxygen or isoflurane in oxygen delivered from a standard anaesthetic machine via a Lack circuit attached to a physiological mouthpiece. Subjects wore a nose-clip and the end-tidal anaesthetic concentration was measured with a Datex Capnomac Ultima. The instrument was switched on for 1 h before use. The instrument was zeroed and the calibrating gas was introduced to give a 0–3% span on the isoflurane channel using Quick Cal calibration gas. Repeat zero and span checks were made throughout the study. Further analysis was made of the instrument accuracy when reading in the 0.06–0.79% range. Samples from the anaesthetic machine fitted with an isoflurane vapourizer and running as oxygen were analysed simultaneously by the Datex Ultima and a Gas S. R. J. TAYLOR, BA, MB, BCHIR, O. A. KHAN, BA, MB, BCHIR, M. L. SWART, FRCA, J. G. JONES, MD, FRCP, FRCA, University Department of Anaesthesia, Addenbrooke’s Hospital, Cambridge, CB2 2QQ. G. G. LOCKWOOD, BSC, FRCA, University Department of Anaesthesia, Royal Postgraduate Medical School, London. Accepted for publication: February 25, 1998. Correspondence to J. G. J. †This was presented to the Anaesthetic Research Society, Bristol Meeting on July 3, 1997.
Neuropsychological function with 0.15% isoflurane

Chromatograph (GC). The GC was calibrated by six gravimetrically prepared primary standards spanning the range 0.06–0.79%. We found that an end-tidal reading of 0.1% on the Ultima was in fact a real concentration of 0.15%. In each case subjects breathed isoflurane until a real constant value of 0.15% end-tidal concentration was achieved. In each case during experimental runs subjects breathed either oxygen or isoflurane in oxygen. It was not possible to blind the subjects to the nature of the respired gas because they could taste the anaesthetic. A stable end-tidal isoflurane concentration reading was achieved for 20 min before the psychological task.

EXPERIMENTAL DESIGN

Sloan letters\(^3\) of height and width 75 mm were displayed in a pseudo-random sequence on a black and white SVGA monitor after audible cues. The Sloan letters are a set of 10 letters (C, D, H, K, N, O, R, S, U, V) designed to be equally visible. The letters displayed were selected from four sets of 10 letters without replacement, and were presented at a luminance differing from that of the background by an amount independently selected from a series of pre-programmed values.

The pre-programmed contrast values were chosen to cover the range of the psychophysical function, so that the subject was always capable of seeing a reasonable proportion of the letter trials fairly easily to maintain subject motivation.

The subject sat approximately 1 m from the screen (note that the exact distance is unimportant\(^4\)), and indicated on the computer keyboard what he thought the identity of the presented letter was. The subject was instructed to guess if he did not know the identity of the letter. Any input that was not one of the 10 Sloan letters was rejected, an audible warning signal was given, and the program waited for a valid input.

Such errors were assumed to be the result of typing mistakes, as all 10 Sloan letters were permanently displayed on the screen. There was no time limit on the subject’s response.

Each series of observations was composed of four “runs” of 50 “trials”, that is, letter presentations, comprising a total of 200 observations, which took approximately 15 min. The letter presented, the subject’s response and the accuracy or otherwise of this response were recorded on the computer’s hard disk.

Two separate presentation protocols were performed. In the first test, the letter was presented at a luminance brighter than that of the background, and remained at this luminance until the subject made a response. This was called the “static” protocol. The second test, the “dynamic” protocol, involved the letter being flashed onto the screen for a period of 1 frame (\(\frac{1}{72}\) s) before disappearing.

HARDWARE

The computer used was a Viglen 486 DX 33 MHz personal computer connected to a SVGA monitor. The 9-pin video card output was modified by feeding the red and blue register outputs into the green output after attenuation by a potential divider circuit to give a black and white output with finer luminance control than usual.

CALIBRATION

The screen was calibrated using a digital photometer. At the beginning of every experiment, the monitor was allowed to warm up for 1 h, in order to eliminate any heat-dependent variations in luminance. The output 0,0,0 (red register, green register, blue register) was then adjusted to a reading of 0.0±0.1 cd m\(^{-2}\) and the output 0,63,0 was adjusted to 100.0±0.1 cd m\(^{-2}\), using the monitor’s contrast control.

The photometer was also used to calibrate the output of the potential divider circuits.

SOFTWARE

A “C” program was written to present the letters and record the results. The program drew the letter and the background at the same luminance at the beginning of each trial. Background and letter luminances were then altered independently. The beginning of a new frame was awaited before any luminance changes were made, in order to avoid the luminance changing over two frames.

ANALYSIS OF RESULTS

Analysis of the results was performed using the Sigma plot scientific graphing software (Jandel Corp.), the contrast sensitivity functions being plotted as probability of correct letter identification against \(\log_{10}\) contrast. The contrast was calculated as the Weber fraction and expressed as a percentage, that is,

\[
\frac{I_{\text{object}} - I_{\text{background}}}{I_{\text{background}}} \times 100\%
\]

where \(I\) represents luminance in cd m\(^{-2}\). Each set of results was modelled to an equation of the

Figure 1  Screen display. A representation of the screen as displayed to the subject. Contrast is defined as: \(\frac{I_2 - I_1}{I_1}\).
general form:

\[ P_c = \frac{0.9}{1 + (kC)^n} \]

where \( P_c \) represents the probability of correctly identifying a letter at contrast \( C \%. \) \( k \) and \( n \) are parameters whose values were determined in an iterative process based on the Marquardt-Levenberg algorithm. The 0.1 and 0.9 terms arise as the function has a minimum of 0.1 and a maximum of 0.1 + 0.9 = 1.0.

The relatively small number of results collected meant that the accuracy of the curve-fit was less certain at the ends of the function, but as only the threshold contrast was used in the comparison of results, this was not significant. Threshold contrast was defined as the contrast at which the subject correctly identified 50% of the letters.

Results

The threshold contrast for each subject with or without isoflurane administration was obtained from a plot of the number of correct letter identifications at a particular contrast level (expressed as a percentage of the total letter presentations at that contrast level) against the contrast level. This is illustrated in figure 2.

The threshold contrasts for the five subjects are plotted in figure 3 for the static protocol and figure 4 for the dynamic protocol.

Isoflurane produced an increase in the threshold contrast of each subject in the static protocol. The increase ranged from 280 to 660% between subjects. Analysis of the curve-fits with the \( F \) test showed significance of the order of \( P < 0.05 \) for each subject between the data obtained with and without 0.15% end-tidal isoflurane.

In the dynamic protocol, an increase in the threshold contrast with isoflurane was also seen in each subject. The increase ranged from 20% to 540%. \( F \) test analysis showed this to be significant at \( P < 0.05 \) for four of the five subjects. In the subject without a significant performance decrease when isoflurane is administered (subject 1 in fig. 4), there appears to be a combination of a below average performance in the absence of isoflurane and an above average performance with isoflurane administration.

Discussion

The results show an increase in the threshold contrasts of all the subjects when isoflurane is administered to give an end-tidal concentration of 0.15%, for both the static and dynamic protocols. There are two possible reasons for this. The first is that the subject’s contrast sensitivity may be affected by isoflurane.
administration. However, it is also possible that isoflurane may induce the subject to make more mistakes when typing in the letter on the keyboard, that is, contrast sensitivity remains unaffected, but input accuracy is reduced.

There are two reasons why it is believed that the effects of alterations in typing accuracy are minimal. First, there are only 10 letter responses that are allowed – if the subject does not pick one of these, he must repeat his choice until he does. This will have the effect of reducing typing errors, although admittedly not all possible errors. The second reason is based on an analysis of the results. If input accuracy were responsible for the change in threshold when isoflurane were administered, the plot of % correct vs contrast would be expected to retain the same sigmoid shape, but to be shifted down the % correct axis. This is because an effect on typing accuracy would be evident along the whole range of the function. However, this pattern is not observed – instead, the curve is shifted to the right, that is, along the contrast axis, implying that it is contrast sensitivity that is the affected factor.

Contrast sensitivity can therefore be confidently said to be a measure of recovery from anaesthetic sedation. In this series of experiments, no attempt was made to assess the dose-dependency of the effect, so it is not possible to comment on the sensitivity of the effect.

Contrast sensitivity may therefore be added to the list of other tests that can be used to measure anaesthetic sedation. The advantage of this technique is the relative simplicity of the equipment required and of the operation of the test – no measuring device needs to be attached to the subject, and the subject’s instructions are easy to follow. The disadvantage of this method is that a fairly large number of results need to be obtained to gain an accurate measurement of contrast sensitivity threshold. In order for a full assessment to be made, some idea of dose-response would be required.

References